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# THE CRYSTAL AND MOLECULAR STRUCTURE OF THE RADIOPROTECTANT CYSTAMINE DIHYDROCHLORIDE

CYSTAMINE dihydrochloride is known to be an effective radioprotectant[1]. Here we report the results of the x-ray analysis of this compound carried out as part of a programme of x-ray investigations on radioprotectants[2–4].

Crystal data : Space group $P2_1/c$

$a = 18{\cdot}15\ (1)$, $b = 4{\cdot}98\ \ (1)$, $c = 20{\cdot}88\ (1)$ Å, $\beta = 143{\cdot}9\ \ (1{\cdot}0)°$, $D_c = 1{\cdot}35$ gm. cm$^{-3}$. As the compound reacted with most of the commonly available solvents, the density could not be measured.

Intensity data from three reciprocal levels *hkl*, $k = 0$ to 2, were recorded by the multiple film equi-inclination Weissenberg method using CuK$\alpha$ radiation. As the only available crystal disintegrated at this stage, further data could not be collected and repeated attempts to recrystallize the sample were not successful. The intensities were estimated visually and this data set contained 476 observable reflections. The incomplete nature of the data set leads to high standard deviations associated with bond lengths and angles. The analysis, however, provides an adequate and reliable description of molecular conformation, especially that about the disulphide bridge, which indeed is its major objective. The crystal structure was solved by a combination of direct methods and Fourier techniques and refined anisotropically to $R = 0{\cdot}122$. The final positional coordinates are given in Table I.

TABLE I

*Final positional coordinates in fractional units* ($\times 10^3$) *and thermal parameters; e.s.d's in parentheses*

| | $x$ | $y$ | $z$ | B (Å$^2$) |
|---|---|---|---|---|
| S (1) | 587 (1) | 231 (4) | 157 (1) | 5·0 |
| S (2) | 538 (1) | 61 (5) | 209 (1) | 4·4 |
| Cl (1) | 858 (1) | 350 (4) | 105 (1) | 4·7 |
| Cl (2) | 122 (2) | 777 (5) | 15 (1) | 7·3 |
| C (1) | 650 (5) | − 48 (15) | 154 (5) | 6·1 |
| C (2) | 773 (6) | −171 (15) | 267 (5) | 6·6 |
| C (3) | 374 (5) | − 57 (15) | 83 (4) | 3·8 |
| C (4) | 302 (5) | 226 (13) | 23 (4) | 3·8 |
| N (1) | 874 (4) | 55 (12) | 338 (3) | 4·5 |
| N (2) | 158 (3) | 132 (13) | −84 (3) | 4·5 |

Figure 1 gives the atomic numbering scheme and a view of the structure along the *b*-axis. The molecular

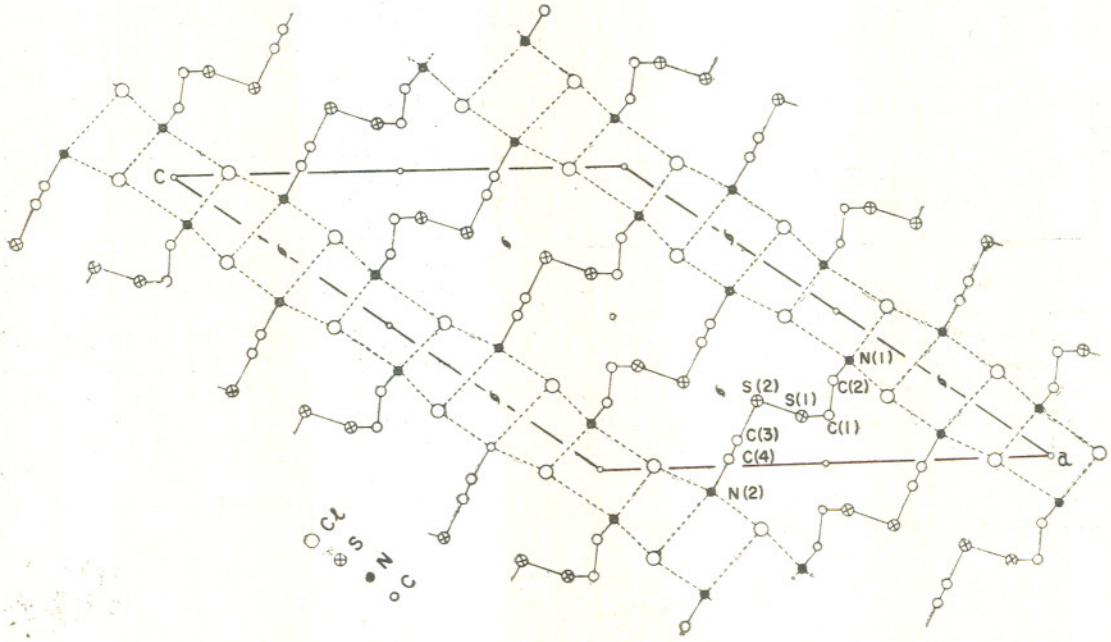


FIG. 1. View of the crystal structure as seen along the *b* axis.

dimensions are listed in Table II. The dimensions of the terminal regions of the molecule deviate substantially from standard values, though the deviations are not significant in view of the large standard deviations. Careful examination of Fourier and difference Fourier maps did not suggest any disorder or modification in the structure. Therefore, it is believed that the abnormal dimensions are due to the poor quality of the data which is well described by the high values of standard deviations.

TABLE II

*Molecular dimensions with e.s.d.'s in parentheses*

| | |
|---|---|
| N (1) — C (2) | 1·56 (9) Å |
| C (2) — C (1) | 1·56 (7) |
| C (1) — S (1) | 1·83 (10) |
| S (1) — S (2) | 2·06 (4) |
| S (2) — C (3) | 1·87 (5) |
| C (3) — C (4) | 1·62 (9) |
| C (4) — N (2) | 1·62 (6) |
| N (1) — C (2) — C (1) — S (1) | — 61 (8)° |
| C (2) — C (1) — S (1) — S (2) | — 65 (7) |
| C (1) — S (1) — S (2) — C (3) | — 89 (5) |
| S (1) — S (2) — C (3) — C (4) | — 66 (5) |
| S (2) — C (3) — C (4) — N (2) | — 178 (5) |
| N (1) — C (2) — C (1) | 108 (7)° |
| C (2) — C (1) — S (1) | 114 (6) |
| C (1) — S (1) — S (2) | 105 (3) |
| S (1) — S (2) — C (3) | 105 (3) |
| S (2) — C (3) — C (4) | 101 (5) |
| C (3) — C (4) — N (2) | 102 (6) |

In the cystamine molecule, the disulphide bond is flanked by linear chains and therefore, the conformation about this bond is unaffected by the steric effects caused by cyclisation or branching in adjacent chains as in most of the other compounds with S-S bond studied so far. Thus the arrangement observed in this structure is likely to represent the intrinsic conformational propensity of an unconstrained disulphide bridge. It, however, turns out that the dihedral angle about the S-S bond has a value in the neighbourhood of 90° as in the derivatives of L-cystine[5]. Even though, the two halves of the cystamine molecule are chemically identical, they have very different conformations. The atoms N (2), C (4), C (3) and S (2) form a planar group, whereas N (1), C (2), C (1) and S (1) do not. S (2) and N (2) in one half of the molecule are *trans* about the connecting C-C bond, whereas the corresponding atoms S (1) and N (1) in the other half are *gauche* about the C-C bond. The *gauche* conformation leads to an intramolecular $NH_3^+ \cdots S$ interaction. Such an intramolecular sulphur-nitrogen interaction has been postulated in Doherty's theory of radioprotection[6] and has also been observed in the crystal structure of another radioprotectant *β*-mercapto ethylamine hydrochloride[7].

The crystal structure consists of layers of cystamine molecules stacked parallel to the *ab*-plane. Both sides of each layer are lined with positively charged amino groups and adjacent layers are connected through chloride ions. The interface between layers involves ionic interactions between amino groups and the chloride ions and NH ··· Cl hydrogen bonds. The nitrogen atom N(1) is surrounded by three chloride ions and the nitrogen atom N(2) by four chloride ions, two of which appear to be involved in a bifurcated hydrogen bond.

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